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EDITORIAL

On these pages the editor offers his opinions, unshackled by advertising patrons and unrestrained by anything save a sense of the decent and the truthful. The editor, alone, is responsible for their type, their tone and their tenor.

"SERENDIPITY"

ON several occasions we have reprinted in this department excerpts or completes of articles appearing in that brilliant Little bulletin, published in the comfortable months by the research laboratories of Arthur D. Little, Inc., of Cambridge, Mass. We say "in the comfortable months" because of a bit of prescript that appears in the current issue, namely: "In accordance with our hot weather custom, the August issue of our Industrial Bulletin will be omitted."

And so, stealing a leaf from their book, we too adopt a hot weather policy and a postponement of mental sweat, by quoting a lot instead of creating a bit.

"Right mistakes" was the paradoxical legend of an editorial appearing in this JOURNAL some years ago. There we recorded how Roentgen happened on his revealing ray; Kekulé on the benzene ring; Nobel, who blundered to his dynamite find, and kidded his master Mars by leaving his fortune to peace; Goodyear, whose rubber researches ended with a successful accident; and how Sweaton mistook a clay for another—yet out of his error grew Eddystone cement, and other cements as well.

The homely wisdom in Samuel Smiles, "Self Help," that "he who never made a mistake—never made a discovery," is thus made more manifest than ever.

The recognition of "right mistakes" is as much a tribute to ingenuity as the too often making of *wrong* mistakes is a sign of inanimity.

And now for Serendipity.

"Pasteur had a true understanding of the mental processes of discoverers and inventors when he stated: 'Chance favors the mind that is prepared.' It is more than a truism that discoveries are made almost exclusively by workers who are keenly searching for an objective. Occasionally the objective may be a bit hazy and at other times

the searcher finds not what he seeks directly but something in its place that may be even more valuable, yet the discovery made is nevertheless an object attained by a search. A special name has been coined for discoveries that differ from what one goes out for; they are instances of 'serendipity—the gift of finding valuable or agreeable things not sought for.'

The term serendipity was recently revived by Dr. W. B. Cannon of the Harvard Medical School in an address reported in the *Scientific Monthly,* entitled 'The Rôle of Chance in Discovery.' The word was apparently first used by Horace Walpole, in 1754, in a letter to his friend Horace Mann, which alluded to an old fairy tale about the 'Three Princes of Serendip' (an old name for Ceylon), who, as they traveled about, 'were always making discoveries, by accident or sagacity, of things they were not in quest of.'

In Dr. Cannon's own field of physiology many serendipitous discoveries have been and still are being made, but always by trained discoverers. The keen physiologist Galvani discovered that frogs' legs suspended by copper wires from the railing of a balcony twitched strangely whenever the free ends touched the iron of the rails as the legs swung in the breeze. By a group of such observations, followed through by study, electricity was gradually brought before the modern mind, via frogs' legs, batteries, static electric generators, Leyden jars, magnets, etc. Very recently, another variant of Galvani's observation of the influence of electricity on nerves is coming to the fore, and nobody yet knows how far physiology and therapy may advance through 'brain waves' and other associations between electricity and the body. Research on the influence of various external conditions on cell-division in eggs led in a roundabout way to the cold therapy which is now being tested as a human cancer treatment.

Archimedes' discovery of the concept of specific gravity is well known. Nobel's discovery of dynamite was also an example of serendipity, as was the finding of the first aniline dye by the boy Perkin, while he was trying to synthesize quinine. One of the most notable chance discoveries was that of America by the navigator, Columbus.

Serendipity is more characteristic of the pioneer than of later workers in any line, but can always occur. Our well-known earth now perhaps affords few opportunities for chance discovery in a geographical way. However, there should continue to be many occasions for the manifestation of serendipity in the developing world of science and industry for a long time to come.

This article was submitted for comment to Dr. Willis R. Whitney, as one of the users and appreciators of the term serendipity. A part of his reply may be of general interest: 'In every individual's stock of knowledge (his conscious and subconscious assets) there lie the peculiar items or records of all his former thoughts. They are permanent records. Some of these may 'pop out' or 'come to mind' when a novel or unexpected event crosses his mental threshold. Some sort of catalysis has taken place. This all indicates dependence of the gift of serendipity upon the total (even forgotten) knowledge and training of the individual. This gives us all a continuing reason for learning more wherever we are.'"

IVOR GRIFFITH.

An Announcement by the American Pharmaceutical Association Committee on Pharmaceutical Research

The A. Ph. A. Committee on Pharmaceutical Research wishes to announce the availability of certain limited funds for research grants.

These grants are to be made by the Council of the A. Ph. A. on the recommendations of the Committee on Pharmaceutical Research. They are to be made on the following basis: (a) The extent which the award will serve to promote pharmaceutical research; (b) whether the award supplements the A. Ph. A. laboratory program; (c) the qualifications of those who will perform the work for which the award is made and the facilities of the laboratory where the research will be conducted; (d) preference will be given to applications wherein the award will supplement a contribution from the institution or laboratory in which the research will be conducted.

Those interested in being considered for the above awards will please make application promptly to the chairman of the Committee on Pharmaceutical Research (Francis E. Bibbins, 150 West Sixty-fourth Street, R. R. 16, Box 728-B, Indianapolis, Indiana) and included in this application should be all the details which will enable the committee to carefully evaluate the projects listed in the application; particularly giving in detail the data mentioned in the above paragraph outlining the basis on which these awards are to be made. These applications should be forwarded promptly so that they can be given consideration before the opening of the college year this fall.

ORIGINAL ARTICLES

OINTMENT VEHICLES FOR ANTISEPTICS*

By Louis Gershenfeld

Professor of Bacteriology, Philadelphia College of Pharmacy and Science

THE ointment bases most commonly used in days gone by and even today by the general practitioner and the dermatologist alike are those which have been prescribed for many decades and are the usual ones official in most pharmacopœias, as petrolatum, lanolin and benzoinated lard.

Petrolatum and similar substances keep for indefinite periods of time. They do not, however, have the power to absorb water. Lard and related compounds possess blandness and softness, but lack in power to absorb water and the quality of remaining unchanged for long periods of time. Lanolin (hydrous wool fat), though possessing the property of tenacity and absorbing water, cannot be kept for long periods of time. Some also object to the odor of Lanolin.

It is difficult to understand why research for more satisfactory ointment vehicles has lagged far behind research for vehicles for medicaments used internally. Those of us who have the occasion to use the older ointment bases are familiar with the greasy appearance imparted to the skin, the fact that our clothing and bed linens become soiled, and the difficulty frequently encountered in the removal of the older bases and medicaments from washable and unwashable materials. Chemistry, pharmacy and medicine have made available substances and methods which make treatments in most branches of therapy convenient, pleasant and efficient. There is no reason why we neglect that branch of therapy in which the use of ointment bases makes possible criticisms by patients and physicians alike. In the final analysis, we must remember that in the use of medicinal ointments, we are concerned mainly with the transmission or absorption of the active agents contained in the ointment bases and not with the absorption of the bases themselves.

*Presented before the U. S. P. Revision Conference preceding the 1940 Pharmacopœial Convention, held May 13, 1940, at Washington, D. C.

An ideal ointment base would be one possessing the following characteristics: stability; neutral in reaction or almost so; non-greasy and not degreasing; non-dehydrating and not too hygroscopic; non-irritating; removable by washing with water; compatible with most all chemicals and body secretions; freedom from objectionable odor; does not stain; capable of having present chemicals soluble in water and in fats and a fairly rapid transfer of such chemicals into the skin; and displaying efficiency on dry, oily and moist skins. One might extend the properties to the ease of preparation and cheapness in cost. The older ointment bases do not meet many of these requirements. However newer ointment vehicles are available which will meet most of these requirements and make possible the more frequent use of ointment bases with increased efficiency. These newer vehicles owe their value due to the presence of substances which act as emulsifying agents and surface tension depressants.

The dermatologist is well aware of the inadequacy of different vehicles for therapeutic agents used in the treatment of skin diseases. Success or failure of therapy in dermatology depends frequently upon physical influences. Among the latter may be the solubility of the active agents or their ionization in the vehicle employed, and the lipotropic or hydrotropic characteristic of the vehicle. The old type ointment bases having an affinity for fat are indicated providing the surface of the skin is relatively intact and fatty. These lipotropic preparations are, however, ineffective if the surface is moist, or as in many cases the epithelial layer of the skin is injured or destroyed. When the latter conditions prevail, a vehicle possessing a hydrotropic characteristic, that is affinity for water is apt to be more effective in bringing the desired active agent or agents in contact with the affected parts of the skin.

Medicinal ointments depend upon diffusion and absorption, primarily, to produce the effects of the active therapeutic agents present. The inclusion of water in ointments has become an important factor, this resulting in a demand for bases that will carry large amounts of water or water-soluble drugs.

Hydrotropic bases, frequently designated as absorption bases, will absorb and carry large amounts of water and water-soluble agents. It is known from the observations of different workers that the therapeutic agents contained in bases with lipotropic characteristics (as lard, petrolatum, anhydrous wool fat) are not absorbed by the skin

as readily as when these agents are contained in hydrotropic bases which hold large amounts of water. The latter absorption bases are marketed as Synthetic Waxes and the Oxycholesterin Bases, which as hydrophilic bases absorb several times their own weight of water.

Oxycholesterin Group

It was Unna who reported in 1912 the isolation of the water-absorbing portion of Lanolin. This portion, a mixture of iso- and oxycholesterins, was found to be a stable and harmless base, possessing in addition to its ability to absorb water the properties of softness and blandness. It contained all of the good qualities present in Lanolin and lacked the objectionable characteristics of the latter. Lifschütz and others succeeded in separating on a large scale the water-absorbing ingredients in Lanolin, and a process of manufacture was presented. As a result, an ointment base consisting of petrolatum containing 3 per cent. of the free alcohols isolated from Lanolin appeared and was recommended as an absorption ointment base. More recently, Powers, Leask and Warner examined the literature concerning Lanolin and the use of its components in hydrophilic ointment bases and revealed the confusion which exists. Their own investigation resulted in the separation of four fractions from the unsaponifiable portion after Lanolin had been saponified. They reported on the amount of water absorbed by mixtures of petrolatum containing separately the four different fractions and petrolatum containing cholesterol with and without cholesterol esters.

Creams made with members of the Oxycholesterin Group are odorless, do not dry out, have long keeping qualities, and are not affected by temperature changes as are other bases. Powers, Leask and Warner state that the emulsifying efficiency of the cholesterol is much less than the emulsifying efficiency of mixtures of cholesterol and cholesterol esters when used with petrolatum for the purpose of emulsifying water. Cholesterol esters when used alone have no emulsifying action. The following trade-marked preparations are products containing cholesterol and cholesterol esters:

1. Aquaphil
2. Aquaphor
3. Eucerin
4. Falba absorption base
5. Lanaform
6. Protegin X
7. Tegolan
8. Thoreps

Waxy Group

The Glyceryl Mono- and Di-Fatty Acid Esters produce oil-in-water type emulsions and are employed in the preparation of neutral oil-in-water non-greasy creams of low and medium fat content. Glyceryl monostearate gives oil-in-water emulsions and is more effective in the presence of soap. It is incompatible with soluble electrolytes and with free organic acid.

The Glycol Fatty Acid Esters contain compounds which appear to be of value as emulsifying agents. Diglycol Stearate, which does not require soap for emulsification, produces a water-in-oil emulsion. Its odor is difficult to mask. It does not absorb much water when mixed with petrolatum. Glycol Glycerol Stearate and Glycol Glycerol Laurate produce water-in-oil emulsions, possess many of the objectionable features of Diglycol Stearate and when used are present in liquid cream preparations. The following members of the Waxy Group, supplied under trade-marked names, belong to the previously mentioned esters:

Tegin (Brand of Glyceryl Monostearate); Tegacid (Tegin treated to withstand the addition of acids and acid-reacting substances); Tegin P (Glycol Monostearate); Tego-Stearate (Glycol Stearate or Diglycol Stearate); Glycosterin (refined Diglycol Stearate); and Xerol (Glyceryl Monostearate). Other fatty acid esters are available and should be investigated.

Ethanolamines

Monoethanolamine, diethanolamine and triethanolamine are colorless or slightly yellowish liquids, available commercially and have found application as mild organic alkalies, solvents, penetrants, dispersing agents, surface-tension depressants, and as intermediates in the preparation of emusifying agents. They and their derivates are miscible with water and in various organic solvents (acetone, alcohol, chloroform and glycerin). Commercial monoethanolamine is a slightly viscous liquid possessing a slight ammonia-like odor, while commercial di- and triethanolamines are syrupy and possess but a faint odor. Many derivatives of the ethanolamines are recorded in the literature but only a few of them have been utilized commercially. Commercial triethanolamine consists of a mixture of approximately 7 per cent. mono-, 18 per cent. di-, and 75 per cent. triethanolamines. The higher

fatty acid salts of the latter, such as the oleates and stearates (in strengths of 2 to 5 per cent.), are efficient emulsifying and dispersing agents for oils, fats, waxes and solvents. Triethanolamine in combination with the soaps formed with the free fatty acids, producing triethanolamine oleate and stearate, is used in the preparation of ointments, which possess the power of absorbing varying amounts of water. As an emulsifier, it permits the use of a large group of vegetable oils, pertoleum products, fats, waxes, etc. which can be emulsified. The resultant product is white in color, possesses a satisfactory consistency and texture, and remains stable for long periods of time. The particles of oil in such an emulsion are of uniformly small size. Vanishing cream formulas containing triethanolamine and triethanolamine oleate or stearate even in low concentration are removed completely by washing. Triethanolamine oleate and stearate produce emulsions of the oil-in-water type and lower surface tension. Mumford claims that triethanolamine extracts natural oil from the skin. This fact and the incompatibilities which occur when certain medicinal agents are present are factors to be considered, and which may mitigate against their universal use.

Higher Fatty Alcohols and Other Compounds

The higher fatty alcohols (cetyl and stearyl alcohols), either alone and especially when in combination with their sulfate and phosphate esters, offer promise as agents which will produce stable emulsions of the water-in-oil type. Hexadecyl and octadecyl (stearyl) alcohols and their phosphated esters are responsible for the properties of HEB, a preparation used in Great Britain and highly regarded as an efficient ointment vehicle. HEB (Halden's Emulsifying Base), made and trade-marked by J. Halden and Co., Ltd. at the suggestion of Dr. P. B. Mumford consists of 3 parts liquid petrolatum, 2 parts white petrolatum, 2 parts of a mixture of higher fatty alcohols (hexadecyl and octadecyl alcohols) containing 10 per cent. acid esters (phosphated) of these alcohols.

Methyl cellulose, forming satisfactory oil-in-water emulsions in liquids as well as other emulsifying agents employed in liquids have not as yet been found capable of admixture to form satisfactory ointment bases.

Action of Water-Miscible Bases

Water-miscible bases are to be preferred as bases for antiseptics and other therapeutic agents when incorporated in the latter to produce ointments, lotions, etc. Self-emulsifying wax and water-miscible vanishing cream bases being miscible can be diluted with water and are comparable to conditions as found in practice on human tissue. Their use results in an "oil-in-water system," the oil being surrounded by the water which is free for circulation and for miscibility with the culture medium or tissue fluids. In such a system electrical conductivity is possible. It is possible to add glycerin or even sufficient fat so as to overcome the drying effect of these bases (if this characteristic is displayed), an objection which occasionally may be raised though many vanishing cream bases do not reveal such an effect. With petrolatum or similar bases, dilution is only possible with oil and not water, as such bases are not miscible with the latter. In the latter system there is no electrical conductivity. With such petrolatum type bases, the medicinal material incorporated with them can escape only with great difficulty into the essentially aqueous environments such as tissue or culture media. When the oxycholesterin type bases are employed, if water is incorporated with the ointment (as it should be), there is provided a water-in-oil emulsion, which, although not miscible with an aqueous fluid, nevertheless, with the proper balance of ingredients, does permit the escape of water in which is dissolved the active medicaments, and this aqueous solution passes into the surrounding medium or environments. Theoretically, one would regard the old ointment bases as the vehicles of choice when ointments containing therapeutic agents are used on skins where sebaceous secretions are present. Practically, however, in many instances ointment vehicles can be used in which the sebaceous secretion is emulsified with the ingredients in the ointment vehicle.

Efficiency of Ointment Bases

Seven years ago, we (Gershenfeld and Miller) reported on the findings of the *in vitro* efficiencies of the different ointment bases, the old and newer types. Within the past year, a more extensive report was published by us (Gershenfeld and Brillhart) on the same subject. We incorporated bactericidal agents in the different vehicles, as with the same antiseptic but different ointment vehicles in the finished

preparations, it was possible to make *in vitro* comparisons of the newer and older bases. Such *in vitro* comparisons with any worthwhile degree of accuracy were not possible with therapeutic agents other than antiseptics. Our tests indicated that antiseptics used in the newer water-miscible ointment bases gave greater bacteriostatic action as revealed by the production of inhibition zones than in the older type of bases when tested by the F. D. A. Agar Plate and Agar Cup Plate techniques.

The following base groups are arranged according to the size of the Inhibition Zones produced—(a) group giving the greatest in width decreasing to (e) the smallest.

(a) Synthetic Wax Base Group
(b) Oxycholesterin Base Group
(c) Benzoinated Lard Group
(d) U. S. P. XI Base Group
(e) Petrolatum Base Group

There was a direct relation in the Inhibition Zones formed within each group, in that the more water the ointment contained the greater was its Inhibition Zone. This relation varied slightly in the Synthetic Wax and Oxycholesterin groups, depending somewhat on variation of ingredients and probably on physical factors.

Though laboratory findings cannot be transplanted to clinical conditions and interpreted always without further observation, the *in vitro* findings we obtained in terms of bacteriostatic action (by noting inhibition zones) appear to be of sufficient value to warrant further study and an extensive clinical investigation of the different newer ointment vehicles. The clinical reports by several practitioners and especially by two prominent dermatologists paralled our *in vitro* findings. They obtained equal valuable results when therapeutic agents other than antiseptics were incorporated in the newer ointment vehicles. In fact, more recently we observed that if the active ingredient responsible as the emulsifier in the newer bases is present in increased amounts, their efficiencies are reduced both in *in vitro* and in *in vivo* tests. This in all probability is due to the fact that the increased amount of emulsifying agent binds the water and does not allow its diffusion from the ointment into the tissues or medium where its action is required. Attention may be directed to the fact that the disappearance of ointments, leaving the skin free from greasiness, may

not be a matter of true absorption. The rate of emulsification must be considered.

It appears that the newer ointment bases are used extensively in the cosmetic industry. Here such factors as appearance, stability and observations when applied to the skin, etc. influence the composition of the formula rather than such factors as effectiveness in the transfer of chemicals into the skin and the efficiency of the preparation on dry, oily and moist skin. It, therefore, should be apparent that empiric formulas may be satisfactory for cosmetic use, but are to be regarded as efficient ointment vehicles for therapeutic agents only after satisfactory *in vitro* and *in vivo* tests are conducted. Though the possibility of allergy due to the use of the newer ointment bases appears remote, a definite answer will be forthcoming only after a wider use of these bases is practiced.

Within the past few days, (after this paper was written), a study of hydrophile ointment bases appeared in an article by Johnston and Lee. Their conclusions were that inasmuch as hydrophile ointment bases containing fairly high amounts of water are sensitive to temperature changes, they were "much less suited to stock ointments than to those for extemporaneous use." There are two points which these workers have overlooked and which should be noted. In the first place, medicaments as ingredients in these bases should be dissolved in the water or oil, depending upon their solubilities and then the ointment emulsion formed. Admixture of the ingredients with the cream base, as they practiced, is not to be recommended as the desirable technique. Secondly, and perhaps more important, we must remember that the water is the dispersed phase in such bases. If stability is the object, as it should be for stock preparations, the dispersed phase should be less than and certainly should not exceed the amount of dispersion medium. If the formula calls for one part of the latter, one should add (as a maximum) not more than one part of water and preferably less than this amount (if stability of the product is of importance). In the investigation of Johnston and Lee, "the water content ranged from 100 per cent. to 300 per cent." Such a high water content will not produce a permanent system since there is considerably more dispersed phase than dispersion medium. This probably accounts for their results and their conclusions. Properly prepared, these bases can be made suitable for stock ointments and will be found to be no more sensitive and perhaps less sensitive to temperature changes than the older ointment bases.

Summary

A brief consideration of the use of the older ointment vehicles is given. Conditions necessary to regard an ointment base as ideal are mentioned. A survey of the newer ointment and absorption bases, in which the active agents are members either of the Oxycholesterin or Waxy groups or are Ethanolamines or members of the Higher Fatty Alcohol group, is presented. The action and efficiency of ointment bases are considered. References are given.

Conclusions

The newer ointment vehicles, including the so-called absorption bases, make possible preparations which are therapeutically more efficient, cosmetically more pleasant, and in general more desirable in most cases than the same preparations prepared with the older bases as the vehicles.

Formulas for these newer ointment bases, as vehicles for antiseptics and other therapeutic agents, should be made available only after they have given satisfactory *in vitro* tests. Such formulas should be continued in use provided reports of *in vivo* tests are satisfactory.

Interpretation of inhibition zones, when such bases containing antiseptics are tested by the F. D. A. Plate and Cup Plate techniques, is suggested as a method of determining the *in vitro* efficiency of ointment vehicles.

Finally, recommendations are made that the Pharmacopœial Revision Committee arrange for a thorough study of "Ointment Vehicles," considering especially the newer absorption bases, present formulas which appear most satisfactory, determine their *in vitro* efficiency, and attempt to obtain wide use of such formulas over the country by dermatologists, who are to be requested to report on the results of their use.

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Announcement of a Study to Evaluate Original Serologic Test for Syphilis

More than five years ago the Committee on Evaluation of Serodiagnostic Tests for Syphilis, in cooperation with the United States Public Health Service, conducted a study to evaluate original serologic tests for syphilis or modifications thereof in the United States. The results of this study were published shortly after the investigation was completed.(1)

Consideration is now being given by the Committee to the organization of a second evaluation study of original serologic tests for syphilis or modifications thereof within the next year. If the need for an investigation of this kind seems to justify the cost, invitations will be extended to the authors of such serologic tests who reside in the United States, or who may be able to participate by the designation of a serologist who will represent them in this country. The second evaluation study will be conducted utilizing methods comparable to those employed in the first study.(2)

Serologists who have an original serologic test for syphilis or an original modification thereof and who desire to participate in the second evaluation study should submit their applications not later than October 1, 1940. The applications must be accompanied by a complete description of the technique of the author's serologic test or modification. All correspondence should be directed to the Surgeon General, United States Public Health Service, Washington, D. C.

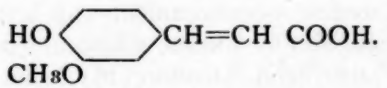
[1] Ven. Dis. Inform., Washington, June, 1935, 16:189; *J. A. M. A.*, Chicago, June 8, 1935, 104:2083.
[2] *J. A. M. A.*, Chicago, Dec. 1, 1934, 103:1705.

PREPARATION AND OXIDATION OF SUBSTITUTED CINNAMIC ACIDS*

By Victor S. Webster

IT was observed in the eighteenth century that when oil of cinnamon was kept for a long period a solid separated. This was at first thought to be benzoic acid, but was later proved by Dumas and Peligot (1) to be cinnamic acid. This acid also occurs in liquid storax, tolubalsam and other plant products, both in the free state and as esters. Its constitution was established by Chiozza (2), and it was first synthesized by Bertagnini (3). Perkin (4) showed that it could be obtained readily by heating a mixture of benzaldehyde, acetic anhydride and anhydrous sodium acetate. This method proved to represent a general reaction and has become known as the Perkin's synthesis, and is specially useful in the preparation of unsaturated acids.

Soon after Perkin's work Tiemann (5) showed that this method was applicable to the synthesis of another naturally occurring compound, viz., ferulic acid.† This was prepared by subjecting vanillin, instead of benzaldehyde, to the Perkin synthesis. In this way ferulic acid was proved to be 3-methoxy-4-hydroxycinnamic acid,



The opportunity to study other closely related compounds has, until recently, been limited due to the lack of the required vanillin derivatives. During the past few years, however, Raiford and coworkers (6) have prepared all chlorine and bromine substitution products of vanillin demanded by theory, and have thus provided starting material for a series of substituted cinnamic acids.

Now it is well known that treatment of a benzene derivative with a carbon side chain with such reagents as alkaline solution of potassium permanganate oxidizes the side chain and leaves benzoic acid.

* Contribution from the Laboratory of Organic Chemistry of the State University of Iowa.

† The name "ferulic acid" refers to an acid of composition $C_{10}H_{10}O_4$, first isolated by Hlasiwetz and Barth [*Ann.*, *138*, 64 (1866)], from Asafoetida, a gum-resin obtained from the rhizomes and roots of several species of ferula.

This oxidation is more easily carried out if the side chain contains an unsaturation, as noted by Tanatar (7) and developed extensively by Baeyer (8). Following the work of Fittig and Ruer (9), cinnamic acid has been oxidized by potassium permanganate under different conditions and several products have been reported. Thus, Smith and Spoehr (10) found that treatment of a pyridine solution of cinnamic acid with enough potassium permanganate to furnish five unit weights of oxygen gave nearly a quantitative yield of benzoic acid. In such a reaction the corresponding aldehyde would probably be an intermediate product, but it would, in most cases, be promptly oxidized further to the acid.

It is an interesting fact that although air alone readily oxidizes benzaldehyde to benzoic acid, as found by Wöhler and Liebig (11), the presence of hydroxyl as a nuclear substituent causes the aldehyde to resist oxidation. For example Bücking (12) and Fittig and Remsen (13) reported that p-hydroxybenzaldehyde and protocatechuic aldehyde, respectively, are not readily oxidized by potassium permanganate solution, but require fusion with caustic potash to give the related acids. Tiemann (14) found that when vanillin, the 3-methyl ether of protocatechuic aldehyde, is treated with oxidizing agents hardly any change takes place or else complete decomposition occurs, depending on conditions; while Brady and Dunn (15) failed to oxidize 5-bromovanillin with acetic acid solution of chromic acid and also by alkaline solution of potassium permanganate. On the other hand, Tiemann (16) found that methyl- and ethyl-vanillin, which contain no exposed hydroxyl, are readily converted to the related acids, though he failed to specify the reagents used and the yields obtained. Later, Tiemann and Nagai (17) reported that oxidation of acetylferulic acid, 3-methoxy-4-acetoxycinnamic acid, gave some acetylvanillic acid and some acetylvanillin. They neglected to mention the oxidation agent used, the conditions under which the work was done, and the yields of the respective products.

In view of the observations noted above it was of interest to study these relations further. This report records some of the results obtained by oxidation of substituted cinnamic acids in which the hydroxyl group in position 4 was covered by an acyl radical.

TABLE I

SUBSTITUTED 3-METHOXY-4-HYDROXYCINNAMIC ACIDS

Substituent in Phenyl Radical	Yield	Solvent	Crystal Form	M. P. ° C.	Formula	Analyses Halogen Calcd.	Halogen Found	Nitrogen Calcd.	Nitrogen Found
2-Bromo-	79	Dilute alcohol	Cream needles	202-203	$C_{10}H_9BrO_4$	29.30	29.39	....	....
5-Bromo-	67	Dilute acetic acid	Pale yellow needles	243-244	$C_{10}H_9BrO_4$	29.30	29.34	....	....
6-Bromo-	73	Dilute alcohol	Pale yellow needles	229-230	$C_{10}H_9BrO_4$	29.30	29.10	....	....
5, 6-Dibromo-	95	Acetic acid	Cream powder	278 (decomp.)	$C_{10}H_8Br_2O_4$	45.45	45.39	....	....
2-Nitro-	70	30% Acetic acid	Yellow needles	210 (decomp.)	$C_{10}H_9NO_6$	....	....	5.85	5.93
5-Chloro-	..	Dilute acetone	Yellow needles	235-236	$C_{10}H_9ClO_4$	15.50	15.89	....	....

Experimental Part

Preparation of cinnamic acids. To convert the substitution products of vanillin into the corresponding cinnamic acids, the Perkin method was used. When the reaction was assumed to be complete the mixture was poured into water, the liquid was heated for a short time and was then neutralized with sodium carbonate solution. Any insoluble material was removed by filtration, and the highly colored filtrate was treated with concentrated hydrochloric acid to precipitate the product. This was collected and purified by crystallization from a suitable solvent. Analytical data and other properties for compounds obtained in this way are given in Table I.

Acylation of the acids. This was done by a slight modification of the method of Pschorr and Sumuleanu (18). A suitable portion of the acid was dissolved in sodium hydroxide solution and to this liquid there was added, with stirring, an ether solution of slightly more than the theoretically required amount of acetic anhydride, while the mixture was agitated until the solid acyl derivative had separated. The product was then removed and crystallized from a suitable solvent. Analytical data and other properties of these derivatives are shown in Table II.

Oxidation of the acyl derivatives. This was done in accordance with the general method of Fittig and Ruer. One gram of the starting material was dissolved in the smallest amount of sodium carbonate solution and the resulting liquid was diluted to a volume of about 100 cc. The solution was then placed in a three-necked flask which was provided with a mechanical stirrer. The flask was surrounded by ice and water, and there was added gradually from a tap funnel a solution of 1.5 g. of potassium permanganate in 75 cc. of water while the mixture was stirred continuously. When the reaction was complete the mixture was filtered to remove manganese dioxide, the filtrate was concentrated to about half its original volume, it was made about neutral by addition of hydrochloric acid, and then evaporated over the steam bath until solid began to separate. More concentrated acid was then added, the mixture was extracted several times with ether, the extract was dried with anhydrous sodium sulfate, the solvent was distilled off and the residue was purified by crystallization from a suitable solvent. The characters of the products and the yields obtained are indicated in Table III.

TABLE II

SUBSTITUTED 3-METHOXY-4-ACETOXYCINNAMIC ACIDS

Substituent in Phenyl Radical	Yield	Solvent	Crystal Form	M. P. ° C.	Formula	Analyses Halogen Calcd.	Halogen Found	Nitrogen Calcd.	Nitrogen Found
2-Bromo-	93	Dilute acetic acid	Cream needles	202-203	$C_{12}H_{11}BrO_5$	25.39	25.34	....	....
5-Bromo-	Nearly quant.	Acetic acid	Colorless needles	212-213	$C_{12}H_{11}BrO_5$	25.39	25.21	....	....
6-Bromo-	95	Alcohol	Colorless needles	211-212	$C_{12}H_{11}BrO_5$	25.39	25.36	....	....
5, 6-Dibromo-	77	Acetic acid	Colorless needles	212-213	$C_{12}H_{10}Br_2O_5$	40.61	40.89	....	....
2-Nitro-	95	Dilute alcohol	Nearly colorless needles	166-167	$C_{12}H_{11}NO_7$	....	....	4.98	5.04
5-Chloro-	Nearly quant.	Acetic acid	Pale yellow granules	201	$C_{12}H_{11}ClO_5$	13.12	13.23	....	....

TABLE III

OXIDATION OF 3-METHOXY-4-ACETOXYCINNAMIC ACIDS

Substituent in Phenyl Radical	Weight of Starting Material, g.	Product Obtained	Yield %
2-Bromo-	1	2-Bromovanillin	27
5-Bromo-	1	5-Bromovanillin	41
6-Bromo-	1	6-Bromovanillin	45
5, 6-Dibromo-	1	5, 6-Dibromovanillin	32
2-Nitro-	1	2-Nitrovanillin	71

Summary

1. Cinnamic acids have been prepared from several substitution products of vanillin. These acids were converted smoothly into good yields of the corresponding acetyl derivatives.

2. Oxidation of these acetyl derivatives with potassium permanganate solution caused the loss of the acyl radical and much degradation occurred. In each case the product that survived was the aldehyde, the original vanillin substitution product. None of the corresponding acid could be isolated.

3. Further work is in progress.

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WHY FOOD LAWS?*

By Howard E. Gensler, P. D., Ph. M.

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YEARS ago when a fight was on for legislation to compel the covering of foods and beverages exposed to street dust, Dr. Charles H. LaWall, noted chemist, who until his decease was associated with the Bureau of Foods and Chemistry of the Pennsylvania Department of Agriculture, had, as he described it, a "prize package" of raisins purchased from a street stand. His report, following analysis of the sample, produced a desired effect on the legislative committee before whom he was called. The raisins were fuzzy with street dust. Besides the raisins he found the following:

Prunes, very dirty.
Beans.
Rice grains.
Dirt so thick on upper surface that the raisins looked fuzzy; numerous hairs visible.
Microscopic examination showed the following:
Hairs, human and animal.
Fragments of animal and vegetable fibres, cotton, wool, etc., dyed green, blue, yellow, brown, pink and gray.
Partly disintegrated bast fibres similar to those from straw, probably from manure.
Partly disintegrated bran fragments, probably from manure.
Sand.
Cornstarch, rice and wheat fragments.
Spores of yeasts and molds.
Pine wood fragments.
Fragments of three other unidentifiable woods.
Unidentifiable vegetable tissue containing spiral ducts.
Tobacco leaf fragments, probably from cigar butts.
Fragment of yellow stained cigarette paper.
Fragment of charred cigarette paper.
Fragment of cigarette tobacco.
Fragments of wings and legs of insects.

Before the days of food laws a report on an examination of milk standing in uncovered pails awaiting their turn to be churned into

* A talk presented before the "Consumer's Group of the Eastern Branch of the American Association of University Women."

butter would have revealed filth just as startling as that found in the raisins. There would, of course, be one difference—the filth in milk would be that native to a barnyard.

In the early period of enforcement of food laws in Pennsylvania a food inspector reprimanded a worker in a candy factory for spitting in a mixing kettle. He suggested that if he just had to spit why not choose the floor—anywhere but the kettle. The worker retorted, "What's the difference between spitting in the kettle or on the floor? The sweepings are dumped into the kettles anyhow."

The General Food Law of Pennsylvania contains a number of provisions intended to restrict and prohibit different kinds of adulteration which it defines. Among them is the provision classing a food as adulterated if it be exposed or kept in a way or manner that might tend to render the article diseased, contaminated or unwholesome. The Department, therefore, requires foods to be covered. You will understand the basis for this requirement when you consider some fundamental consideration of possible dangers latent in uncovered foods.

When you stand in front of uncovered candy and say to the clerk, "*P*lease give me *t*en cents worth of *th*is candy," the air immediately in front of your mouth is thrown into violent motion. Pronunciation of the letter "p" and of the letter "t" causes a veritable cyclone of air particles to issue from the mouth. Actual photographs made by employing the "Tyndall effect" have demonstrated this to be true. Therefore, germs of cold, pneumonia or other diseases are actually sprayed for a distance of several feet from the mouth. A sneeze on uncovered goods, as shown by photographs, produces an air disturbance almost unbelievable. Bacteria of all kinds must be scattered like so many seeds.

It would be horrifying to contemplate what goes on when an ordinary house fly makes a landing on food. A recent article in the "Reader's Digest" on "Our Enemy, the Fly," is a good answer to "Why Protect Foods from Contamination." I quote: "From egg to adult has taken less than ten days. And this adult fly is ready immediately for breeding. If a female, in less than a week it will probably lay its first batch of 100 or more eggs, repeating at ten-day intervals. In view of this speed, and of the house fly's vast fecundity, it becomes apparent how huge the tribe would grow were it unchecked. Nine generations is average in the season from mid-April

to September. The offspring of a single pair of house flies in that time, if all lived, would amount to the astronomical figure of 335,923,200,000,000 flies. The adult house fly's life is no prettier spectacle for the squeamish than was its infancy. Its prime concern is food. It relishes with equal enthusiasm decaying garbage or other filth and the lumps of sugar on your dinner table. And it flies directly from one kind of food to the other, a disturbing fact in view of its highly specialized anatomy and physiology.

In the first place, its entire body is covered with a tangle of fine, close-growing hairs; and similar hairs grow on wings, legs and feet. The fly is thus equipped with the finest of catchalls. In the second place, there is the extraordinary structure of its feet. Each foot is equipped with an adhesive pad of sticky hairs. It is by means of these that the fly negotiates slippery polished surfaces so nimbly and can walk upside down on ceilings; but it is also by means of these sticky pads that it picks up and transmits myriad germs.

Furthermore, the mouth parts of the house fly are a pair of soft, fleshy lobes at the end of its proboscis. There is no chewing mechanism. (The flies that bite you sometimes in muggy weather are not house flies, but another variety called cabanids.) Accordingly, a fly can feed on a lump of sugar only by first softening it. To do this the fly regurgitates on the sugar a drop of fluid from its last digested meal. It is this gruesome antic that the fly is performing at our dinner table when he seems to be exploring the sugar bowl; these regurgitated droplets, together with the insect's excreta, make up the "flyspecks" that are every housewife's plague.

Such, then, is the life story of the fly—a creature born and matured in filth, and uniquely equipped for transmitting that filth wherever it may go. Its danger to man can hardly be overstated. "In the case of more than thirty different disease organisms," says Dr. L. O. Howard, consulting entomologist of the United States Public Health Service, "laboratory proof exists that they are carried by the fly." Doctors and writers in medical journals, likewise have repeatedly and emphatically pointed out its great menace to national health. Careful tests have shown that the bacteria on the hairy body of a single fly may number as many as five million and that a single buzzing *Musca domestica* can infect a whole household.

So, when Dr. LaWall made his report on the filth found in uncovered raisins he was battling for law to make it a criminal offense

and prevent the sale of food inadequately protected from contamination of the kind we have just cited. The General Food Law provides that a person found guilty of this form of violation must pay a fine of sixty dollars for his negligence.

Agents of the Bureau of Foods and Chemistry go from store to store demanding that foods be covered. Many times storekeepers resent the order and consider it just another whim. After considering such facts as we have just presented, the Bureau not only enforces the letter of the law, but does so knowing it to be a duty necessary for public health. I believe you must approve.

Another requirement of the General Food Law has far reaching benefits. I refer to the clause which makes it unlawful to make an article appear of better or greater value than it is by any means.

I well remember how hucksters used to sell their strawberries—big, sound, tempting, strawberries. I refer to the ones on top. After the huckster disappeared—the deception was discovered—strange it was that the little berries just happened to be on the bottom.

Quite sometime ago there was devised a clever means to make milk appear of better quality than it actually was by making a deep cream line. It was done this way—the cream was skimmed from the milk and whipped in a special and very expensive machine to a much increased volume. It was then put back with the already skimmed milk. Apparently there was more cream than actual analysis showed —some of this milk contained half as much cream as regular milk not thus fabricated. Arrests could be made because of the "better or greater value" clause in the law.

Another cheater decided to increase his sales of hamburger. His idea put into action was lots of suet, some meat and a red light. The meat looked unusually attractive to women purchasers and the butcher actually increased his sales. The red light was a means of making the meat look better than it was—a violation deserving a fine.

To make foods appear better or of greater value than they are is a temptation some food manufacturers or dealers have not learned to overcome. Here are a few of their means and devices—packing olives in glass that magnifies and makes them look bigger; wrapping popcorn in yellow transparent paper to lend appearance of cheese or more cheese; wrapping bakery products in amber transparent paper to make them appear as rich in certain ingredients; adding pumpkin, squash, coal tar color, carrots or carotene to rolls or cakes to deceive

Mrs. Housewife to believe them rich in butter or eggs; having "Vanilla" in big, prominent letters and the word "imitation" so small and inconspicuous that it isn't seen; using bottles with their sides pressed in so that they must be higher to contain the little liquid that is in them; putting oranges in colored mesh bags to make them appear more golden; packing tissue paper in boxes of popcorn to fill up some of the space of a long box; stuffing sausages in red colored casings to make them look like richer in meat and so on. Why food laws?

There is another clause in the General Food Law, little but powerful, making substitution of a substance or ingredient for the article purchased a criminal offense. This provision becomes effective and useful in many instances. I can imagine your surprise to learn that a barker at a fair would offer his customers canned dog meat under the name "hamburger sandwich"—substitution. In butter we have found as high as 45 per cent. of water substituted for butter. Water at twenty cents a pint! The violators paid so many fines that they finally requested the Department to excuse them from wasting the time taken to attend aldermen's hearings—just let them send their fines in every week without the hearings!

In sausages, we know commonly as frankfurters, substitution on the part of a few dishonest meat packers would go on to limits we cannot imagine were it not for restraining food laws. Frankfurters, sausages or bologna should be ground meat mixed with seasoning—not water mixed with meat. The Pennsylvania Sausage Law limits the amount of water in frankfurters or sausages. Nevertheless, the state continues to find excessive water, sometimes as high as 70 per cent. Then there are the fillers—milk powder, cereal flour, soya flour and gums that swell up and make the frankfurter or bologna look prosperous—all substitutes for meat.

Recently an agent of the Department paid $2 for a can labeled olive oil. The following statements—most of them false—were on the can:

> Italian Produce Sublime Olive Oil.
> Imported by Acomo Fo Lucca.
> The Olive Oil contained in this can is pressed from fresh picked high grown fruit, packed by the grower under the best sanitary condition, and guaranteed to be absolutely pure under any chemical analysis. The producer begs to recommend to the consumer to destroy this can as soon as empty in order to pre-

vent unscrupulous dealers from refilling it with adulterated oil or oil of an inferior quality.

The producer warns all such dealers that he will proceed against them to the full extent of the law.

Analysis showed that the can contained cottonseed oil, not olive oil, as claimed. The "substitution" provision of the law is effective in punishing violations of this type.

As reasons for food laws we could refer to the many volations found since such laws have been passed. This would not be feasible or advisable. Only several of the many provisions of the General Food Law have thus far received reference in this paper. There are many others equally important which will not be discussed at this time.

Twenty-eight laws govern the sale of foods in Pennsylvania. Included among these laws is the Advertising Law. The others pertain to specific products such as butter, cheese and eggs and other foods. The Department of Agriculture is charged with the enforcement of the food laws. The Bureau of Foods and Chemistry, a division of the Department, conducts this enforcement. With your indulgence, we shall consider several other provisions of the General Food Law the application of which is vital in their importance to the buying public.

According to the General Food Law it is illegal to offer for sale or to sell contaminated foods. Let us see how this works out in practice. If you were on a jury in a court case, would you condone the sale of contaminated food? Assume that the arrest was made for the sale of fruit still containing arsenic or lead spray residue. It might be your first experience as a juror. According to rules of evidence the state might not be permitted to give testimony on its knowledge of the danger in eating foods containing lead gained by previous experience. Our testimony would have to be confined to the case being tried. Thus you might be convinced by the defense that the action was unwarranted. Consider your failure to support the Commonwealth in the light of the following clipping taken from one of our daily newspapers: "Karl Woehrman, 11, of Juneau, Wis., whose left eye was afflicted with a rare disease when he ate a poison-sprayed apple, returns to America after going alone to Germany and back for a rare operation that was never performed because his doctor had been called to military service."

The General Food Law confers on the Department of Agriculture the power to make such rules and regulations it deems necessary to enforce the law. The law refers to "contaminated," and the Department must define and decide when an article of food is contaminated under that authority. This it only does after due consideration of all angles of the problem. If an arrest is made because of the presence of lead you may be sure that there is plenty of precedent and reason for it.

Huckleberries may not be considered "contaminated" if they contain an occasional maggot. However, when there are as high as fifteen in a quart and if they are big and juicy, something should be done about it—they are contaminated. Who would question that?

Trichinae are intestinal parasites common in pork transferable to man and causing the serious disease known as trichinosis. Now, no butcher or anyone else can pick these "worms" out of the pork they sell. The trichinae are not harmful if the pork is properly cooked. It is only reasonable and necessary, therefore, that the customer know when he is given pork, when he has asked for hamburger, so that the precaution of cooking it thoroughly may be taken. The undeclared addition of pork to fresh beef may be construed as an act of contamination. In this connection I quote the following from the "Annual Report of the Department of Public Health, Commonwealth of Massachusetts, for the year ending November 30, 1938." "At the close of the fiscal year a sample of hamburg steak containing pork was collected in western Massachusetts. At the hearing given the company, the representative asked how we knew it contained pork. He was informed that first, the inspector, who is a competent meat man, noticed it; second, he asked the store manager why he put pork in the hamburg steak, and the store manager responded that he used up his pork ends in that way; and in the third place, the chemist had separated the fat crystals and had obtained samples of stearin crystals, which, by their microscopic appearance came from pork fat and pork fat only. This case will result in a prosecution early in the next fiscal year.

It is unfortunate that so many meat men will put pork into hamburg steak. This material is assumed by the consuming public to be beef. It is frequently eaten rare and is very rarely cooked to a temperature sufficiently high to kill trichinosis. It is possible that the apparent increase in trichinosis in this part of the country may be

due to this practice of adding pork to hamburg steak without distinctly notifying the customer to that effect."

It is interesting to note that none of the food laws state how adulteration or misbranding is to be determined. Chemistry or chemical analysis is not mentioned. Yet, enforcement would not be possible without chemistry. All the cunning and science of chemistry is called upon to determine composition, adulteration, misbranding as well as other factors necessary to decide whether these laws are violated. The microscope, the polariscope, ultra-violet light, the photo-electric cell, the refractometer, the cryoscope, the spectroscope and many other scientific instruments, are employed in the battle to detect the cheater.

"Why Food Laws?" We answer, to protect your health and your pocketbooks. "Wherefore spend your money for that which is not meat?" The Bureau examines everything used as food from chewing gum to watermelons. As a result you very rarely find some of the following former practices: ice cream whipped up to an unfair volume; rotten or partly germinated eggs going into pound cake; "orange juice" that isn't orange juice; cereal, color, soy, preservatives, milk powder in sausages; teaseed oil, cottonseed oil and other cheaper oils in olive oil; moulds, yeasts, color and thickeners in tomato products; color, lack of eggs, decomposed eggs, soya and carotene color in noodles. There are examples ad infinitum.

The primary object of the food laws is the protection of public health. This protection not only embraces the possibility of the presence of harmful or poisonous substances, but takes into account nutritive aspects of articles of diet. Foods can be manufactured in such a manner as to be practically valueless for nourishment. Coal tar flavor, coal tar color, saccharin, water and carbon dioxide may make a delicious "cherry soda," but furnish no food value. Oleomargarine lacks butter fat vitamins necessary to health—a good reason for action. Yellow coal tar color will not take the place of hen's eggs. On taking such situations into account, food laws are assets to public health.

Your pocketbook also enters the matter of food control. When a fourteen-carat ring is sold as an eighteen-carat ring, the purchaser has lost money. Equally wrong or worse is the sale of water for the price of butter or meat as is the case when water is worked into either. Your money spent for food should be honored. You should

receive the article for which you ask. A dinner special advertised as "Twenty-five Cent Chicken Dinner" was ordered by a customer and he got Lebanon County pork pudding. The customer was cheated. You may lay down five cents for a bottle of Coca Cola and be given some other "cola." It is the function of Pennsylvania food laws to prevent these things.

Pennsylvania can well be proud of the lead it has taken in vindicating the necessity of food laws. Its activities in enforcement of food laws is a good answer to the subject, "Why Food Laws?" She ranks high, if not highest, among the states in food law enforcement. Often violators of food laws declare they "are sorry it happened—the food was never intended to be sold in this state—it got into Pennsylvania by mistake." Violations are the exception rather than the rule because our laws are effective and enforced to the full extent of the Department's resources.

We intend not only to keep Pennsylvania heading the list as a matter of pride, but for the protection of its citizens in respect to the purity, quality and value, dollar for dollar, whenever and wherever sale of food is involved.

The Vitamin K Activity of 4-Amino-2-Methyl-1-Naphthol and 4-Amino-3-Methyl-1-Naphthol. A. D. Emmett, O. Kamm and E. A. Sharp. *J. Biol. Chem. 133,* 285 (1940). Considerable interest has been shown in potent water soluble vitamin K preparations. The authors report the preparation of various compounds two of which appear most promising in this respect. These substances, 4-amino-2-methyl-1-naphthol and 4-amino-3-methyl-1-naphthol as the hydrochlorides are readily soluble in water and can be given either orally or parenterally. The former is almost three times as effective when tested on chicks as the vitamin K_1. Clinically it has been found to give excellent results. Daily doses ranging from 3600 to 7200 curative chick units given intravenously restored to normal severe prothrombin deficiency of obstructive jaundice within two to three days. Infants have responded within twelve hours to a dosage of 1800 units as have dogs with severe prothrombin depletion induced by biliary fistula. L. F. T.

COMMON RED SPIDER DAMAGE TO DIGITALIS PURPUREA

By A. F. Sievers*

THE common foxglove, *Digitalis purpurea,* which is so widely grown as an ornamental in its various forms, is perhaps the best example of a plant that is not only popular in the home garden but provides one of the most important of medicines. The several preparations made from the leaves of digitalis are practically indispensable in present-day medical practice and any circumstances that interfere with the growing of the plant may, therefore, have a much deeper significance than may appear to those who are interested only in the plant as an ornamental.

There are usually three sources of digitalis leaves available in normal times to the manufacturers of medicinal digitalis preparations: (1) Imports from Europe; (2) cultivated plants grown by such manufacturers to meet their own requirements, and (3) collection of the plant in the wild state in the Pacific Northwest. Normally the first-mentioned source is perhaps the most important. These imports have ranged in the period 1932-1938, inclusive, from 32,764 to 80,652 pounds. Regarding the amount obtained from the other sources, no statistics are available, but these sources can be drawn upon more extensively if the imports of the drug are interfered with. Such a situation developed during the World War and as a result digitalis and other essential botanical drugs were placed under cultivation in this country for the period of the emergency.(1). Perhaps a similar situation may come about as the result of the present conditions in Europe.

It has generally been considered that digitalis is one of the easiest medicinal plants to grow and, in fact, experience supports this view. However, in the past five years it has been impossible to grow this plant in the Medicinal Plant Garden of the Bureau of Plant Industry at Arlington, Virginia, near Washington, D. C., on account of damage by the common red spider, *Tetranychus telarius* (Linn.).(2). The infestation usually begins with the advent of warm weather and all plants, large and small and in the first and second year of growth are attacked. In the last few years most of the plants have been completely killed by the end of the first season or at least the damage has been so severe that no leaf crop could be obtained. No leaves were entirely free from damage and even where the damage was least the effect on the appearance of the leaves was such that they would not

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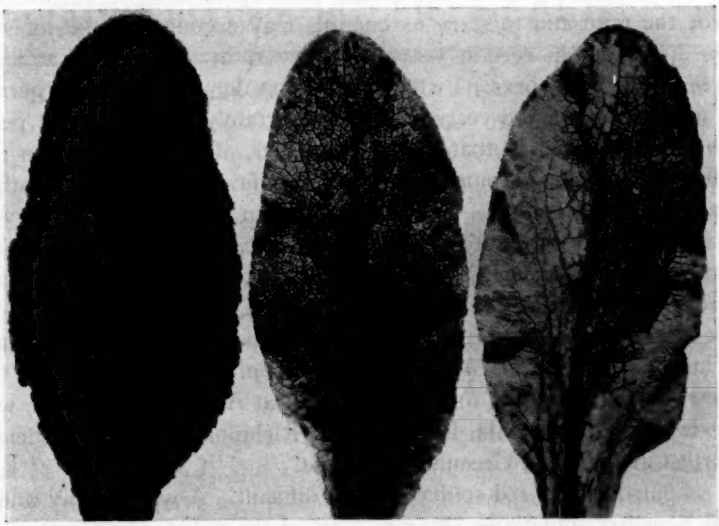
be acceptable to the trade. The photograph shows, left, normal leaf; center, partly damaged; and right, badly damaged leaf.



The wide distribution of digitalis in nurseries, on seed farms, and in home gardens and the equally wide distribution of the spider mite would certainly justify the expectation that damage to the plant from this cause would be very common indeed but, strangely enough, this apparently is not the case.(3). In view of the complete loss experienced at Arlington Farm, the writer made inquiries in 1937 among persons thought to be in a position to observe the plant growing in reasonable sized plots concerning instances of such damage and the seriousness thereof. Either a photograph or a pressed specimen of a badly damaged leaf was sent with each inquiry. To such inquiries 18 replies were received in eight of which it was stated that no such damage had ever been experienced although in several cases observations extended over many years. Three reported minor damage had been noted occasionally and four appeared to have definitely encountered trouble from this cause. In two of these four the correspondents commented that the damage had been noted only in the previous two years (1935 and 1936), and one of those who reported minor damage also had observed it for the first time in the previous season (1936). The question naturally arises, in view of these comments,

whether the infestation of the plants in such localities may be on the increase and that it may in time become as severe as at Arlington Farm. Certain weather conditions, especially drought, apparently favor the mite and to some extent this may account for the infestation appearing in certain years. However, in the case of at least three of the eight persons who reported no damage at all the period of observation was 18 years or more. Certainly many drought periods have occurred in that time. Moreover, at Arlington Farm the damage has been so complete that no significant relation to weather conditions is suggested. The eight cases in which no damage was reported included two from Philadelphia, Pennsylvania, and vicinity, two from Los Angeles, California, and one from Galesburg, Michigan, Madison, Wisconsin, Minneapolis, Minnesota, and Boulder, Colorado. The three instances of minor damage were reported from Boston, Massachusetts, Atlanta, Georgia, and Madison, Wisconsin, while the more severe infestation, in addition to that at Arlington, Virginia, was observed at Philadelphia, Pennsylvania, Richmond, Virginia, Raleigh, North Carolina, and Greenfield, Indiana.

Control of the red spider is often difficult. A water spray under high pressure sometimes removes most of the mites. Information in regard to the control of this pest may be obtained by writing the Bureau of Entomology and Plant Quarantine, U. S. Department of Agriculture, Washington, D. C. It is intended to undertake some experiments the coming summer on the control of this pest on digitalis plants under field conditions. In the meantime the writer will be glad to hear from others who have observed damage from this cause. It is especially desirable to hear from persons who have opportunity to examine the plant in the wild state in the Pacific Northwest.

REFERENCES

1. A brief history of commercial medicinal plant culture in the United States. Mimeograph, Division of Drug and Related Plants, Bureau of Plant Industry, U. S. Department of Agriculture.

2. Identification by H. E. Ewing, Bureau of Entomology and Plant Quarantine, U. S. Department of Agriculture. The species which has long gone under the name of *Tetranychus telarius* (Linn.) is currently known as *T. bimaculatus* (Harvey).

3. Specialists in the Bureau of Entomology and Plant Quarantine of the Department state that the literature does not record any injury to digitalis by the spider mite. They believe that because this pest is so common and feeds on such a wide range of plants those who have observed it on this plant may have assumed that its occurrence had already been recorded. Personally these specialists have noted the mite occurring on digitalis in a commercial perennial planting near Rochester, New York, and an infestation at Huntington, West Virginia, was also noted.

ABSTRACTS FROM AND REVIEWS OF THE LITERATURE OF THE SCIENCES SUPPORTING PUBLIC HEALTH

Balsam of Peru in Ointments. E. Bridon. *Un. Pharm. Paris 80,* 225 (1939) through *Quart. J. Pharm. and Pharmacol. 13,* 84 (1940). A perfectly smooth ointment can be obtained by triturating 20 gm. of the balsam with about 10 gm. of chloroform until solution is effected and then mixing with 80 gm. of white petrolatum. The product is beaten occasionally until all odor of chloroform is removed. This concentrated ointment containing 20 per cent. of the balsam can be used for the rapid preparation of other ointments containing the balsam as a constituent.

Stability of Bacteria in Relation to pH. J. G. Baumgartner and G. G. Knock. *J. Soc. Chem. Ind. 59,* 53 (1940). The authors considering bacteria as protein systems investigated the stability of five different species of bacteria, namely, *Esch. coli, Esch cloacæ, Proteus vulgaris, Staph. aureus* and a *Lactobacillus* insofar as the optimum pH was concerned. The stability was judged based on (a) heat resistance, (b) precipitation with ethyl alcohol, and (c) flocculation as measured by the opacity of the bacterial suspension. Except with the Lactobacillus, which was grown on wort-agar, the others were obtained from twenty-four-hour agar cultures. Distilled water was used to remove, wash and suspend the organisms. The suspensions were agitated for five minutes and filtered through cotton plugs to remove clumps. A phosphate-citric acid buffer was used, diluted 1 in 2½, and 100 cc. quantities were prepared for each pH value from 3.0 to 8.0. The heat treatment was carried out by adding 1 cc. of the properly diluted aqueous suspensions of the bacteria to 25 cc. of the buffer solutions, and, after mixing 3 cc. of each suspension, they were heated in thin-walled tubes in a water bath. After rapid cooling in water 1 cc. of the suspension and 1 cc. of a 1-1000 dilution were plated.

For the alcohol treatment 5 cc. of absolute alcohol were added to 20 cc. amounts of the buffer solution, the pH adjusted if necessary, and the pH checked electrometrically at the end of the experiment. The organisms were added to the alcohol-buffer mixture and held at

22 degrees C. At the end of the exposure 1 cc. portions were placed in 19 cc. of sterile water and plates prepared.

The stability in suspension was tested by taking thick suspensions of the bacteria in the buffer solution in tubes, holding at 40 C. for twenty-four hours and then visually evaluating the degree of opacity and sedimentation. The optimum value was taken as that tube in which opacity was maximal and sedimentation minimal.

In each test the optimum pH for stability was about the same for a given species of organism. The results are tabulated as follows:

	Heat resistance	Alcohol resistance	Stability of suspension
E. coli	6.4	6.4	6.4
E. cloacæ	6.0-6.4	6.0	6.0-6.4
Proteus vulgaris	6.0	6.0	6.0
Staph. aureus	7.2	7.2	6.8-7.2
Lactobacillus	5.2	5.2	5.2-5.6

The authors conclude that thermal resistance, stability in the presence of alcohol and stability in suspension are interrelated by one important factor—hydration. The next part of the problem to be undertaken is the electrochemical behavior of the five species in relation to pH value.

L. F. T.

The Solvent Action of Various Substances on Teeth. J. W. Trask, E. E. Ziegler and E. C. Maloof. *J. A. D. A.* 27, 1013 (1940). The etiology of dental caries is not completely understood. There are both intrinsic factors such as vitamin intake, mineral salts, race, heredity, etc., as well as extrinsic factors such as dentifrices, food and drink, the chemical factors of the saliva and the products of the bacterial flora.

There seems to be among dentists a firm belief based on long experience that acids in general are harmful to teeth, causing decalcification and thus paving the way for decay. The acid most frequently mentioned in this connection is lactic acid and the fermentation of carbohydrates in the mouth by Lactobacillus acidophilus, producing lactic acid, is generally believed today to be the chief cause of caries.

Certain authors have already presented evidence that foods containing citric acid can cause decalcification of teeth. In this investigation the solvent actions of a number of acids such as citric, phos-

phoric, lactic, acetic, tartaric, etc., were quantitatively determined as well as some alkalies, sugars and various waters. Pieces of tooth of uniform size were subjected to a five-day slow percolation with the n/10 or m/10 acid, base or sugar, and the loss in weight determined at the end of the process.

The acids had the most marked effect in dissolving the tooth, the amount dissolved increasing rapidly with a drop in pH. Thus n/10 citric having a pH of 2.3 dissolved 78.8 per cent. The alkalies showed no significant solvent action on tooth. Waters had very little effect although distilled water dissolved more than tap water, probably due to its lower pH. Sugars preserved with thymol (1-1000) dissolved practically no tooth substance, but when no preservative was present there sometimes occurred some fungus or bacterial growth with resulting increase in solvent action.

It is pointed out that foods which are excessively acid are not used by primitive tribes that have a low incidence of dental caries and that neither are they used by animals. L. F. T.

Results in the Treatment of Acute Poliomyelitis with Antistreptococcic Serum. E. C. Rosenow. *Minn. Med. 23,* 161 (1940) through *Squibb Abstr. Bull. 13,* 412 (1940). The treatment of a group of 221 patients suffering with poliomyelitis with a poliomyelitis antistreptococcic serum resulted in a mortality of only 4.5 per cent. and an incidence of severe residual paralysis in only 3.3 per cent. of the cases. The control group of 116 patients had a mortality of 19.8 per cent. and an incidence of severe residual paralysis in 34.4 per cent. The serum employed was 1 part of the centrifuged euglobulin fraction of the antiserum of horses hyperimmunized with heat-killed poliomyelitis streptococcus dissolved in 9 parts of normal salt solution and containing 0.2 per cent. of phenol. It was injected intramuscularly once or twice daily in 5-20 doses depending on age, severity of symptoms and the results obtained. The degree of residual paralysis was in direct proportion to the duration of time from the onset of the disease to the administration of the serum, severe and moderate paralysis occurring when this time was an average of 4.3 or more days no paralysis occurring when this time was 2.3 or less days. The serum administration causes almost immediate benefits, lowering the temperature, lessening pain, halting progressive paralysis and aiding the restoration of lost muscular function. L. F. T.

BOOK REVIEW

Done by persons, unafraid to upbraid, but perfectly willing to give praise where praise is really due.

The Law of Drugs and Druggists. (Second Edition.) By William R. Arthur, Professor of Law, University of Colorado; 577 pages. West Publishing Co., St. Paul, Minn. 1940. Price $3.00.

This new edition is intended not only as a text for students of pharmacy but also as a quick and easy reference for retailers, wholesalers, and manufacturers. The wording is clear and understandable to the layman, explaining not only the legal rights of the pharmacist but also his numerous liabilities as a professional man, business man and employer.

The new provisions of the Federal Food, Drug and Cosmetic Act as well as the restrictions on advertising contained in the Wheeler-Lea Act are brought into the text.

Many legal questions are listed, followed by the answer in terms of a case which is cited and then briefly set forth together with the point of law employed in rendering a decision.

The book is supplemented by an excellent index making possible the quick finding of many questions arising in the legal field relating to pharmacy.

L. F. TICE.

The Use of Silver Acetate Solution in the Prophylaxis of Ophthalmia Neonatorum. W. F. Hartman. *Pennsylvania Med. J. 43,* 639 (1940). The use of a 1 per cent. solution of silver acetate in place of silver nitrate is recommended in the Credé method for the prevention of ophthalmia neonatorum. The use of silver acetate in 3315 cases resulted in only an incidence of the infection in 0.09 per cent. Chemical conjunctivitis was produced in only 2.1 per cent. of cases as compared with 4.3 per cent. when silver nitrate was used. An advantage of the use of silver acetate is that there is no danger of administering too strong a solution as sometimes happens with the nitrate since a 1 per cent. solution is saturated. L. F. T.